

10/534824

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
3 June 2004 (03.06.2004)

PCT

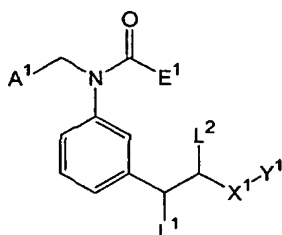
(10) International Publication Number
WO 2004/046162 A3

- (51) International Patent Classification⁷: **C07C 233/61**
- (21) International Application Number:
PCT/US2003/036195
- (22) International Filing Date:
14 November 2003 (14.11.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/426,456 14 November 2002 (14.11.2002) US
60/491,185 29 July 2003 (29.07.2003) US
- (71) Applicant (*for all designated States except US*): **THE SCRIPPS RESEARCH INSTITUTE** [US/US]; 10550 North Torrey Pines Road, La Jolla, CA 92037 (US).
- (72) Inventors; and
(75) Inventors/Applicants (*for US only*): **NICOLAOU, Kyriacos, C.** [US/US]; 9625 Blackgold Road, La Jolla, CA 92037 (US). **ROECKER, Anthony, J.** [US/US]; 3337 Clairemont Dr., #4, San Diego, CA 92117 (US). **HUGHES, Robert** [GB/US]; 800 N. Lindberg, Q403, Creve Couer, MO 63167 (US). **PFEFFERKORN, Jeffrey, A.** [US/US]; 1521 Natalie Lane, Apt. #202, Ann Arbor, MI 48105 (US).
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:
— with international search report
- (88) Date of publication of the international search report:
12 August 2004
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*



WO 2004/046162 A3

(54) Title: NON-STEROIDAL FXR AGONISTS



(I)

(57) Abstract: ABSTRACT Potent non-steroidal farnesoid X receptor (FXR) agonists are N-aryl-N-arylmethyl amido and ureido compounds having the chemical structure represented by the following formula (I): INSERT FORMULA wherein E1 is (C1-C8)alkyl, cyclohexyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, phenyl, or NH(C1-C8)alkyl; L1 and L2 are both H, or together form a pi-bond; X1 is C(O), or CH2; Y1 is H, NHZ1, NH(Z2)Z3, or OZ4; aryl moiety A1 is selected from the group of radicals consisting of: INSERT FORMULA A2 and G1 - G11 are as defined in the specification; and T1 and T2 are each independently O, S, NH, or N(C1-C8)alkyl. The FXR agonists are useful as therapeutic agents for the treatment

of diseases linked to cholesterol, bile acids, and their metabolism and homeostasis.

CORRECTED VERSION

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
3 June 2004 (03.06.2004)

PCT

(10) International Publication Number
WO 2004/046162 A3

(51) International Patent Classification⁷: C07C 233/61

(21) International Application Number:
PCT/US2003/036195

(22) International Filing Date:
14 November 2003 (14.11.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/426,456 14 November 2002 (14.11.2002) US
60/491,185 29 July 2003 (29.07.2003) US

(71) Applicant (for all designated States except US): THE
SCRIPPS RESEARCH INSTITUTE [US/US]; 10550
North Torrey Pines Road, La Jolla, CA 92037 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): NICOLAOU,
Kyriacos, C. [US/US]; 9625 Blackgold Road, La Jolla,
CA 92037 (US). ROECKER, Anthony, J. [US/US];
3337 Clairemont Dr., #4, San Diego, CA 92117 (US).
HUGHES, Robert [GB/US]; 800 N. Lindberg, Q403,
Creve Couer, MO 63167 (US). PFEFFERKORN, Jeffrey,
A. [US/US]; 1521 Natalie Lane, Apt. #202, Ann Arbor,
MI 48105 (US).

(74) Agents: CEPURITIS, Talivaldis et al.; OLSON & HI-
ERL, LTD., 20 North Wacker Drive, 36th Floor, Chicago,
IL 60606 (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK,
MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT,
RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR,
TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,
SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM,
GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:

— of inventorship (Rule 4.17(iv)) for US only

Published:

— with international search report

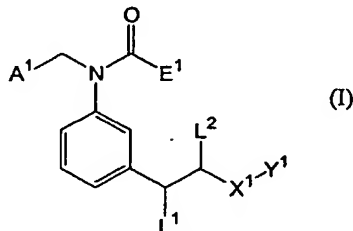
(88) Date of publication of the international search report:
12 August 2004

(48) Date of publication of this corrected version:
24 March 2005

(15) Information about Correction:
see PCT Gazette No. 12/2005 of 24 March 2005, Section II

For two-letter codes and other abbreviations, refer to the "Guide-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: NON-STEROIDAL FXR AGONISTS



(57) Abstract: ABSTRACT Potent non-steroidal farnesoid X
receptor (FXR) agonists are N-aryl-N-arylmethyl amido and
ureido compounds having the chemical structure represented
by the following formula (I): INSERT FORMULA wherein
E1 is (C1-C8)alkyl, cyclohexyl, 2-furyl, 3-furyl, 2-thienyl,
3-thienyl, phenyl, or NH(C1-C8)alkyl; L1 and L2 are both
H, or together form a pi-bond; X1 is C(O), or CH2; Y1 is H,
NHZ1, NH(Z2)Z3, or OZ4; aryl moiety A1 is selected from the
group of radicals consisting of: INSERT FORMULA A2 and
G1 - G11 are as defined in the specification; and T1 and T2 are

each independently O, S, NH, or N(C1-C8)alkyl. The FXR agonists are useful as therapeutic agents for the treatment of diseases
linked to cholesterol, bile acids, and their metabolism and homeostasis.